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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/234,290	01/20/1999	LINDA C. BURKLY	10274/008003	6288

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BOSTON, MA 02110

EXAMINER

UNGAR, SUSAN NMN

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 07/15/2003

27

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/234,290

Applicant(s)

Burkly

Examiner

Ungar

Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on March 11, 2003 and June 17, 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 25 and 31-35 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 25 and 31-35 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☒ Interview Summary (PTO-413) Paper No(s). 2
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

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1. Upon review and reconsideration the Finality of the previous Office Action is withdrawn.
2. The Appeal Brief filed on March 11, 2003 (Paper No. 23) in response to the Letter of January 27, 2003 is acknowledged and has been entered. The Amendment-After-Appeal submitted on June 17, 2003 (Paper No. 24) is acknowledged and has been entered. Claim 25 has been amended and claims 28 and 36 have been canceled. Claims 25, 31-35 are currently under prosecution.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

3. Claims 25, 31-35 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention.

The claims are drawn to a method of treating insulin dependent diabetes comprising administering to a prediabetic mammal or a mammal having partial beta cell destruction, a composition comprising a soluble fibronectin polypeptide comprising the EILDV motif in an amount effective to treat diabetes. The specification teaches that some promising results with immunosuppressive agents have been seen in clinical trials for the treatment of diabetes, however, the agents have toxic side effects (p. 3, lines 16-35), thus there is a need for safe immunosuppressive components which inhibit entry of effector cells into the pancreas or function of those cells which may have already entered the islets of

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Langerhans, for use in the prediabetic stage (p. 4, lines 17-24). The specification teaches that the present invention provides a method for the prevention of insulin dependent diabetes comprising the step of administering to a prediabetic individual, a VLA4 blocking agent including a soluble VCAM-IgG fusion protein, an anti VLA-4 antibody as well as fibronectin and fibronectin peptides containing the EILDV motif. VLA-4 is expressed on lymphocytes (p. 2, lines 12-14), that is B cells and T cells which are effector cells known to be involved in autoimmune cellular destruction. These agents block VLA-4 by competing with the cell surface binding protein for VLA-4 or by otherwise altering, inhibiting or blocking VLA-4 function (p. 5, lines 1-20) The specification teaches that administering an anti-VLA-4 antibody significantly reduced the incidence of diabetes in a well established NOD mouse model of diabetes (p. 4, lines 15-25) and that a VCAM-Ig fusion inhibits the onset of diabetes in an adoptive transfer model in NOD mice (p. 29, lines 19-25).

One cannot extrapolate the teaching of the specification to the enablement of the claims because the data from the antibody and VCAM construct cannot be extrapolated to the enablement of the claimed method using the claimed soluble fibronectin polypeptide. Applicant has argued that since the specification provides guidance to enable VLA-4 inhibitors in the claimed method, any and all VLA-4 inhibitors, including the currently claimed soluble fibronectin polypeptide will also function in the method as claimed. However, Ryan et al (J. Clin. Invest., 1991, 88:995-1004) specifically teach that VLA-4 has two known ligands, fibronectin and VCAM-1 and that they interact with VLA-4 at distinct binding sites (p. 1001, col 2).

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Although, consistent with the data of the instant application, anti-VLA-4 antibody as well as anti-VCAM-1 antibody inhibited VLA-4 dependent binding/adhesion of immature B cells to bone marrow-derived fibroblasts (see abstract, p. 995), neither blocking antibodies to fibronectin nor a soluble fibronectin fragment FN-40 containing the VLA-4 binding site (the EILDV motif) inhibited binding/adhesion of the B cells (p. 1001, col 2). Further, van Dinther-Janssen et al (J. Rheumatology, 1994, 21(11)1998-2004) teach that type B synovial lining cells of patients with rheumatoid arthritis express VCAM-1 as well as fibronectin (Abstract). Again, although consistent with the data of the instant application, anti-VLA-4 antibody as well as anti-VCAM-1 antibody inhibited VLA-4 dependent binding/adhesion of T cells to type B synovial lining cells, the CS1 fibronectin fragment did not inhibit VLA-4 dependent binding of the T cells to type B synovial lining cells (see Figure 6, page 2002, col 1). Examiner takes note that fibronectin CS1 comprises the EILDV motif (see Yamamoto et al, Anti-Cancer Drugs, 1994, 5:424-428, p. 424, col 2).

Although it is known that VLA-4 binds both fibronectin and VCAM, it is clear that the claimed soluble fibronectin polypeptide is not an inhibitor of VLA-4 dependent binding of precursor B-cells to bone marrow-derived fibroblasts or an inhibitor of VLA-4 dependent binding of T cells to type B synovial lining cells of rheumatoid arthritis patients. Given the above, no nexus has been established between the VLA-4 inhibitory activity of the anti-VLA4 antibody/VCAM-1 construct and the claimed soluble fibronectin polypeptide. Thus, it is reasonable to

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conclude a nexus does not exist and therefore, it is clear that it cannot be predicted from the information in the specification that the invention will function as claimed. The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art and no evidence has been provided which would allow one of skill in the art to predict that the method would function as claimed with a reasonable expectation of success. For the above reasons, it appears that undue experimentation would be required to practice the claimed invention. Applicant is invited to submit objective evidence demonstrating that the claimed soluble fibronectin polypeptide functions as claimed.

4. All other objections and rejections in Paper No. 17 are withdrawn.
5. No claims allowed
6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Ungar, PhD whose telephone number is (703) 305-2181. The examiner can normally be reached on Monday through Friday from 7:30am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached at (703) 308-3995. The fax phone number for this Art Unit is (703) 308-4242.

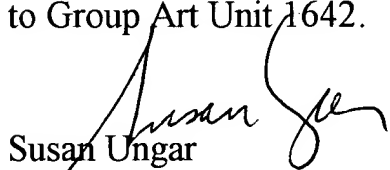
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

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Effective, February 7, 1998, the Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1642.



Susan Ungar

Primary Patent Examiner

July 9, 2003



ANTHONY C. CAPUTA
SUPERVISORY PATENT EXAMINER
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